

## REMARKS

Claims 1-7 and 10-21 are now in the application. Claims 8 and 9 have been cancelled without prejudice or disclaimer. Claims 1 and 20 have been amended to recite “wherein the water-soluble impurity is a reducing agent used for converting oxidized coenzyme Q<sub>10</sub> into reduced coenzyme Q<sub>10</sub> and/or an impurity derived from the reducing agent, the reducing agent being selected from the group consisting of hyposulfurous acid, hyposulfurous acid salts, ascorbic acids, esters of ascorbic acids and salts of ascorbic acids, the ascorbic acids being selected from the group consisting of ascorbic acid, rhamno-ascorbic acid, arabo-ascorbic acid, gluco-ascorbic acid, fuco-ascorbic acid, glucohepto-ascorbic acid, xylo-ascorbic acid, galacto-ascorbic acid, gulo-ascorbic acid, allo-ascorbic acid, erythro-ascorbic acid and 6-desoxyascorbic acid. Basis for the amendments to claims 1 and 20 can be found at page 9, line 32 to page 10, line 9 and page 20, lines 19-30 of the specification. Claim 10 has been amended to depend from claim 1 and to recite that the reducing agent “is selected from the group consisting of ascorbic acids, esters of ascorbic acids, salts of ascorbic acids, the ascorbic acids being selected from the group consisting of ascorbic acid, rhamno-ascorbic acid, arabo-ascorbic acid, gluco-ascorbic acid, fuco-ascorbic acid, glucohepto-ascorbic acid, xylo-ascorbic acid, galacto-ascorbic acid, gulo-ascorbic acid, allo-ascorbic acid, erythro-ascorbic acid and 6-desoxyascorbic acid”. Basis for the amendments to claim 10 can be found at page 20, lines 19-30 of the specification. Basis for newly presented claim 21 can be found at page 23, lines 3 to 17 of the specification. The amendments to the claims and newly presented claims do not introduce any new matter.

The rejection of claim 10 under 35 USC 112, second paragraph has been overcome the above amendment to claim 10 that recites specific ascorbic acids and esters or salts of ascorbic acids in place of the term “ascorbic acid or a related compound thereof”.

Claims 1-20 were rejected under 35 USC 103(a) as being unpatentable over GB 947643 to Merck et al. and applicants’ acknowledged prior art in view of US Patent 4,061,660 to Kijima et al., US Patent 4,039,573 to Kijima et al. and US Patent 4,163,864 to Morita et al. The cited references fail to render obvious the present.

Before addressing the rejection over the cited art, a discussion of the present invention would be helpful. In particular, the present invention is directed to a process of purifying reduced coenzyme Q<sub>10</sub>. According to the present invention, a water-soluble organic solvent or a mixed solvent composed of a water-soluble organic solvent and water is used to wash crystals and/or oil of reduced coenzyme Q<sub>10</sub>, and a water-soluble impurity derived from the reducing agent such as hyposulfurous acid or ascorbic acids is thereby removed. The distinctive feature of the present invention is that a water-soluble organic solvent or a mixed solvent composed of a water-soluble organic solvent and water is used for washing. In order to remove impurities highly soluble in water such as hyposulfurous acid, ascorbic acids and derivatives thereof, those skilled in the art would use water for washing. However, as already explained in the previous response, impurities cannot be sufficiently removed when water is used for washing crystals and/or oil of reduced coenzyme Q<sub>10</sub>. Even those skilled in the art would not expect that water-soluble organic solvents are much more effective than water for removing water-soluble impurities. Although it is not known exactly why water is unsuitable for washing, it is believed that a sufficient amount of water cannot arrive at or contact impurities existing between crystals and/or oily portions of the reduced coenzyme Q<sub>10</sub>, which has a poor wettability against water (please see page 2, lines 24 to 25 of the specification).

Further, washing of the crystals and/or oil should be distinguished from washing of the solution. If a solution is washed with a washing solvent, it is necessary that the solution and the washing solvent are separable. However, depending on the reaction solvent used for the reduction of oxidized coenzyme Q<sub>10</sub>, it is impossible to wash the solution. For example, in Production Example 1 of the present application, oxidized coenzyme Q<sub>10</sub> is reduced in ethanol. It is impossible to wash the reaction solution containing ethanol without carrying out an additional process such as replacement of ethanol with another solvent.

Even if the solution and the washing solvent are separable, washing of the solution is not favorable in a large-scale production since a large quantity of washing solvent is required and also it is troublesome and difficult to separate a liquid phase from the other liquid phase after the washing process.

According to the present invention, washing can be carried out regardless of the reaction solution and also the washing solvent and the desired product can be easily separated since the crystals and/or oil are/is washed.

GB 947643 fails to suggest the present invention since, among other things, as appreciated by the examiner, GB 947643 does not even imply washing of the crystals. Moreover, the product therein, as recognized by the examiner, would necessarily contain water-insoluble impurities such as the reducing agent and/or derivatives derived from the reducing agent. The secondary references do not overcome the deficiencies of GB 947643 with respect to rendering unpatentable the present invention.

The office action does not provide the adequate rationale or reasoning as to why persons skilled in the art would wash crystals and/or oil with a water-soluble organic solvent. As already discussed in the previous response, the secondary references do not teach washing crystals.

In Example 1 of US Patent 4,061,660 to Kijima et al, the reaction mixture contained silica-alumina (please see Col. 4, lines 40 to 43), and after filtration the silica-alumina was washed with diethyl ether to remove and collect a desired product which adhered to the surface of silica-alumina. Accordingly, those skilled in the art would readily understand that the procedure suggested therein does not include washing of crystals or oil of a desired product for removal of impurity.

In Example 3 of US Patent 4,039,573 to Kijima et al., the filtrate was washed with water and then with a weak-caustic soda aqueous solution. Namely, the reference teaches washing the solution of a desired product. The procedure does not include washing of crystals or oil of a desired product for removal of impurity as required by the present invention.

In Example 1 of US Patent 4,163,864 to Morita et al., the filtrate was washed with a methanolic aqueous sodium hydroxide solution and then with an aqueous methanol solution (please see col. 4, lines 31 to 36). Therefore, the reference teaches washing the filtrate

liquor, namely a solution of a desired product. The procedure does not include a washing of crystals or oil of a desired product for removal of impurity as required by the present invention.

Since the secondary references are silent about impurities derived from hyposulfurous acid, hyposulfurous acid salts, ascorbic acids, esters of ascorbic acids or salts of ascorbic acids and since they do not disclose washing crystals or oil , it is not at all apparent why the cited references would render obvious the present invention. The rejection relies upon impermissible “hindsight”.

In the office action, the examiner commented concerning possible comparative experiments. However, since the examiner has not even made out a *prima facie* case of obviousness, such comparative experiments are not actually needed in this application. Please see *Takeda v. Alphapharm*, 492 F. 3<sup>rd</sup> 1350 (Fed. Cir. 2007).

Accordingly, the present invention is not rendered obvious GB 947643 to Merck et al. in view of US Patent 4,061,660 to Kijima et al., US Patent 4,039,573 to Kijima et al. and US Patent 4,163,864 to Morita et al.

In view of the above, consideration and allowance are respectfully solicited.

In the event the Examiner believes an interview might serve in any way to advance the prosecution of this application, the undersigned is available at the telephone number noted below.

Application No.: 10/541,446

Docket No.: 21581-00496-US

The Office is authorized to charge any necessary fees to Deposit Account No. 22-0185, under Order No. 21581-00496-US from which the undersigned is authorized to draw.

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